(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 23 October 2003 (23.10.2003)

PCT

(10) International Publication Number WO 03/087160 A1

(51) International Patent Classification⁷: C07K 14/75, A61K 38/17, A61P 7/00

(21) International Application Number: PCT/NL03/00293

(22) International Filing Date: 7 April 2003 (07.04.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 1020426 18 April 2002 (18.04.2002) NL

(71) Applicant (for all designated States except US): NED-ERLANDSE ORGANISATIE VOOR TOEGEPAST-NATUURWETENSCHAPPEIJK ONDERZOEK TNO [NL/NL]; Schoemakerstraat 97, NL-2628 VK Delft (NL).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): DE MAAT, Monica, Petronella, Maria [NL/NL]; Mathenesserlaan 249, NL-3021 HD Rotterdam (NL). KOOLWIJK, Pieter [NL/NL]; Rottumstraat 4, NL-1825 NM Alkmaar (NL).
- (74) Agent: PRINS, A.W., Nieuwe Parklaan 97, NL-2587 BN Den Haag (NL).

- (81) Designated States (national): AE, AG, AL, AM, AT (utility model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, ES, FI (utility model), FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK (utility model), SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

A1

OF CELLS

(54) Title: MODIFICATION OF THE PROPERTIES OF A FIBRIN MATRIX WITH RESPECT TO GROWTH AND INGROWTH

(57) Abstract: A method for modifying the properties of a fibrin matrix relative to growth and ingrowth of cells, wherein for forming the fibrin matrix a fibrinogen is used consisting of a selected fibrinogen variant or a fibrinogen enriched or depleted in a selected fibrinogen variant. In particular, the use of high-molecular weight (HMW) fibrinogen leads to a fibrin having accelerated angiogenesis properties, while the use of low-molecular weight (LMW and/or LMW') fibrinogen leads to fibrin having decelerated angiogenesis properties. The use of HMW fibrinogen when setting up angiogenesis tests results in that the tests require less time. Fibrin sealants on the basis of HMW fibrinogen can be used for burns, to promote wound healing or to inhibit scar tissue. Fibrin sealants on the basis of LMW or LMW' fibrinogen are useful to inhibit adhesions and tumor growth, for instance after surgical operations.



THIS PAGE BLANK (USPTO)

INTERNATIONAL SEARCH REPORT

		PCI/NL 0	3/00293
A. CLASSII IPC 7	FICATION OF SUBJECT MATTER C07K14/75 A61K38/17 A61P7/0	0	
According to	International Patent Classification (IPC) or to both national classific	cation and IPC	
	SEARCHED		
Minimum do IPC 7	cumentation searched (classification system followed by classificat $C07K-A61K$	tion symbols)	
	ion searched other than minimum documentation to the extent that		
	ata base consulted during the international search (name of data b		ed)
MEDLIN	E, BIOSIS, EPO-Internal, WPI Data,	EMBASE	
	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with Indication, where appropriate, of the re	elevant passages	Relevant to claim No.
A	EP 1 142 581 A (AMERICAN NATIONA CROSS) 10 October 2001 (2001-10- the whole document	1-24	
A	WO 00 72852 A (BRISTOL MYERS SQU COMPANY) 7 December 2000 (2000-1 the whole document	1-24	
А	WO 98 55140 A (OMRIX BIOPHARMACEUTICALS) 10 December 1998 (1998-12-10) the whole document		1-24
		-/	
			-
1			
			0
X Furth	ner documents are listed in the continuation of box C.	Patent family members are lists	ed in annex.
° Special ca	tegories of cited documents :	"T" later document published after the ir	temational filino date
	ent defining the general state of the art which is not lered to be of particular relevance	or priority date and not in conflict wi cited to understand the principle or	th the application but
"E" earlier o	document but published on or after the international	invention "X" document of particular relevance; the	e claimed invention
filing d	ant which may throw doubts on priority claim(s) or	cannot be considered novel or canno involve an inventive step when the	ot be considered to document is taken alone
citation	is cited to establish the publication date of another norther special reason (as specified)	"Y" document of particular relevance; the cannot be considered to involve an	inventive step when the
other r		document is combined with one or r ments, such combination being obvi in the art.	nore other such docu-
"P" docume later th	ent published prior to the International filing date but an the priority date claimed	"&" document member of the same pater	nt family
Date of the	actual completion of the international search	Date of mailing of the international s	earch report
<u> </u>	September 2003	10/09/2003	
Name and n	nailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2	Authorized officer	
	NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Moreau, J	

INTERNATIONAL SEARCH REPORT

PCT/NL 03/00293

		 700293
C.(Continua Category o	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HINSBERGH VAN V W M ET AL: "ROLE OF FIBRIN MATRIX IN ANGIOGENESIS" ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, NEW YORK ACADEMY OF SCIENCES, NEW YORK, NY, US, vol. 936, 2001, pages 426-437, XP008011814 ISSN: 0077-8923 the whole document	1-24
A	DEMPLFE C-E ET AL: "FIBRINOGEN HETEROGENEITY IN HOMOZYGOUS PLASMINOGEN DEFICIENCY TYPE I: FURTHER EVIDENCE THAT PLASMIN IS NOT INVOLVED IN FORMATION OF LMW- AND LMW'-FIBRINOGEN" THROMBOSIS AND HAEMOSTASIS, STUTTGART, DE, vol. 77, no. 5, May 1997 (1997-05), pages 879-883, XP008011824 ISSN: 0340-6245 the whole document	1-24
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 22 March 2002 (2002-03-22) HALLEMEESCH MARCELLA M ET AL: "The turnover rate of HMW fibrinogen to LMW fibrinogen determines the plasma profile of these proteins." Database accession no. PREV200200369325 XP002226013 abstract & FASEB JOURNAL, vol. 16, no. 5, 22 March 2002 (2002-03-22), page A788 Annual Meeting of Professional Research Scientists on Experimental Biology; New Orleans, Louisiana, USA; April 20-24, 2002, March 22, 2002 ISSN: 0892-6638	1-24
A .	COLLEN ANNEMIE ET AL: "Aberrant fibrin formation and cross-linking of fibrinogenNieuwegein, a variant with a shortened Aalpha-chain, alters endothelial capillary tube formation." BLOOD, vol. 97, no. 4, 15 February 2001 (2001-02-15), pages 973-980, XP002226021 ISSN: 0006-4971 the whole document	1-24

1

INTERNATIONAL SEARCH REPORT

Information on patent tamily members

PCT/NL 03/00293 I

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
EP 1142581	A	10-10-2001	EP	1142581 A2	10-10-2001
,	••		ÃΤ	212554 T	15-02-2002
			AU	. 667188 B2	14-03-1996
			AU .	9109391 A	25-06-1992
			CA	2097063 A1	28-05-1992
			DE	69132918 D1	14-03-2002
			DE	69132918 T2	31-10-2002
			DK	· 564502 T3	13-05-2002
			EP	0564502 A1	13-10-1993
			JP	6506191 T	14-07-1994
			WO	9209301 A1	11-06-1992
			US	6197325 B1	06-03-2001
			US	6117425 A	12-09-2000
			US US	6054122 A	25-04-2000
			US	6559119 B1	06-05-2003
WO 0072852	Α	07-12-2000	AU	5458800 A	18-12-2000
			CA	2373704 A1	07-12-2000
			EP	1187623 A1	20-03-2002
			JP	2003500170 T	07-01-2003
			NO	20015759 A	29-01-2002
			MO	0072852 A1	07-12-2000
WO 9855140	Α	10-12-1998	AU	8336098 A	21-12-1998
			WO	9855140 A1	10-12-1998

THIS PAGE BLANK (USPTO)